

CLAIMS

1. A DNA molecule comprising an expression system capable, when transformed into a recombinant host, of producing the C140 receptor at the cell surface of the 5 host, which expression system comprises a nucleotide sequence encoding the C140 receptor operably linked to a control sequence heterologous to said encoding nucleotide and operable in said host cell.

2. A cell modified to contain the expression 10 system of claim 1.

3. A method to produce cells that contain C140 receptor deployed at their surface, which method comprises culturing the cells of claim 2 under conditions which effect the expression of the nucleotide sequence 15 encoding the C140 receptor to obtain said cells that contain C140 receptor deployed at their surface.

4. A cRNA molecule that encodes the C140 receptor.

5. Cells which are oocytes modified to 20 contain the cRNA of claim 4.

6. A method to produce cells which are oocytes that contain C140 receptor deployed at their surface, which method comprises culturing the oocytes of claim 5 under conditions which effect the expression of

P A T E N T
Atty Dkt: 2803-0006.20

51 -

the cRNA encoding the C140 receptor to obtain said cells
that contain C140 receptor deployed at their surface.

7. A method to determine the C140 agonist
activity of a candidate substance, which method comprises:
5 incubating the cells of claim 3 or 6 in the
presence and absence of the substance, and
detecting the presence, absence or amount of
activation of the C140 receptor in the presence as
compared to the absence of said substance whereby an
increase in said activation in the presence as compared to
the absence of said substance indicates agonist activity

8. A method to assess the ability of a
candidate substance to behave as a C140 antagonist, which
method comprises:
15 incubating the cells of claim 3 or 6 in the
presence of a C140 agonist and in the presence and absence
of said candidate, and
20 measuring the activation of the C140 receptor
in the presence and absence of said candidate, whereby a
decrease in said activation in the presence of the C140 receptor
candidate indicates the antagonist activity of the
candidate.

9. A method to assess the ability of a
candidate substance to bind to C140 receptor, which method
comprises:
25 incubating the cells of claim 3 or 6 in the
presence of a C140 antagonist and in the presence and absence
of said candidate, and
measuring the activation of the C140 receptor
in the presence and absence of said candidate, whereby a
decrease in said activation in the presence of the C140 receptor
candidate indicates the antagonist activity of the
candidate.

2803-0006.20-183-620.APP

- 52 -

incubating the cells of claim 3 or 6 in the presence of a C140 agonist or a known C140 antagonist and in the presence and absence of said candidate, and measuring the binding of said C140 agonist or 5 C140 antagonist to the surface of said cells in the presence and absence of said candidate, whereby a decrease in said binding in the presence of the candidate indicates the ability of the candidate to bind receptor.

10. An antibody composition specifically 10 immunoreactive with an extracellular region of the C140 receptor protein or a portion thereof.

11. The antibody composition of claim 10 wherein said region is the ligand-binding region, or which is specifically immunoreactive with 15 activated C140 receptor, or recognizes an epitope within the receptor sequence SLIGRL, or is specifically reactive with the cleaved activation peptide of the C140 receptor.

20. 12. A method to localize activated C140 receptors *in situ*, which method comprises: administering to a subject putatively harboring activated C140 receptor an amount of antibody specific to said activated receptor effective to bind to said 25 activated receptor, and detecting the location of said antibody.

- 53 -

13. A method for detecting the presence of activated C140 receptor in a mammalian subject, which method comprises:

5 contacting a sample of the biological fluid of said subject with a detection system which measures the presence, absence or amount of the cleaved activation peptide of the C140 receptor; and

detecting the presence, absence or amount of said cleaved peptide.

10 14. An agonist peptide capable of activating C140 receptor, which peptide is of the formula

AA₁-AA₂-AA₃-AA₄-AA₅-AA₆-AA₇-Z (1)

wherein AA₁ is a small amino acid or threonine; AA₂ and AA₃ are each independently 15 neutral/nonpolar/large/nonaromatic amino acids; AA₄ is a small amino acid; AA₅ is a basic amino acid; AA₆ may be present or absent and, if present, is a neutral/nonpolar/large/nonaromatic amino acid; 20 AA₇ is absent if AA₆ is absent and may be present or absent if AA₆ is present, and is an acidic amino acid; and Z is a substituent that does not interfere with agonist activity.

- 54 -

15. The peptide of claim 14 wherein AA₁ is ser, ala, gly, thr, or 2,3-diamino-propionic (2,3-diaP); and/or

wherein each of AA₂ and AA₃ is independently selected from the group consisting of ile, val, leu, and Cha; and/or

wherein AA₄ is Gly; and/or

wherein AA₅ is Arg, Lys or Har; and/or

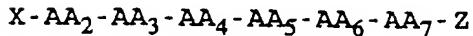
wherein Z comprises OR', or NR'R' wherein each 10 R' is independently H or is a straight or branched chain alkyl or 1-6C, wherein each R' may optionally be substituted with one or more substituents selected from the group consisting of -OR', -NR'R', and -NR'CN'R'NR'R' wherein each R' is H or is a straight or branched chain 15 alkyl of 1-6C.

16. The peptide of claim 15 wherein AA₁-AA₂-AA₃ is selected from the group consisting of SLI, SLL, SChal, SChal, (2,3-diaP)LI and (2,3-diaP)LL; and/or wherein Z includes additional peptide sequence 20 of 1-5 amino acids.

17. The peptide of claim 14 which is selected from the group consisting of SLIGRLETQPPIT, SLIGRLETQPP, SLIGRLETQPP, SLIGRLETQ, SLIGRLET, SLIGRLE, SLIGRL, SLIGR, SLLGKVDGTSHT, SLLGKVDGTSHV, SLLGKVDGTSH, 25 SLLGKVDGTS, SLLGKVDGT, SLLGKVDG, SLLGKVD, SLLGKV, SLLGK, S(Cha)IGR, S(Cha)LGK, (2,3-diaP)-LIGR, (2,3-diaP)LLGK, SLLGKR-NH₂, SLIGRR-NH₂, S(Cha)LGKK-NH₂, S(Cha)IGRK-NH₂, (2,3-diaP)-LIGRK-NH₂, and (2,3-diaP)-LLGKK-NH₂.

- 55 -

18. A peptide capable of inhibiting the function of the C140 receptor which peptide is of the formula



5 wherein X is an amino acid residue other than ser, ala, thr, cys, 2,3-diaP or gly or is a desamino or acylated amino acid,

wherein AA₂ and AA₃ are each independently neutral/nonpolar/large/nonaromatic amino acids;

10 AA₄ is a small amino acid;

AA₅ is a basic amino acid;

AA₆ may be present or absent and, if present, is a neutral/nonpolar/large/nonaromatic amino acid;

15 AA₇ is absent if AA₆ is absent and may be present or absent if AA₆ is present, and is an acidic amino acid; and

Z is a substituent that does not interfere with agonist activity.

19. The peptide of claim 18 wherein X is Mvl, 20 Mpr, Mba, or SMeMpr; and/or

wherein each of AA₂ and AA₃ is independently selected from the group consisting of ile, val, leu, Nle, Nva, Cyclopentylalanine and Cha; and/or

wherein AA₄ is Gly; and/or

25 wherein AA₅ is Arg, Lys, Orn or Har; and/or

wherein Z comprises OH or an ester or salt thereof, or NR'R' wherein each R' is independently H or is

- 56 -

a straight or branched chain alkyl of 1-6C, wherein each R' may optionally be substituted with one or more substituents selected from the group consisting of -OR', -NR'R', and -NR'CN'R'NR'R' wherein each R' is H or is a straight or branched chain alkyl of 1-6C.

20. The peptide of claim 19 wherein AA₂-AA₃ is selected from the group consisting of LI, LL, ChaI, and ChaL; and/or

10 wherein Z includes a peptide extension of 1-5 amino acid residues.

21. The peptide of claim 18 which is selected from the group consisting of Mpr-LLGK, Mpr-LIGR, Mpr-(Cha)LKG, Mpr-(Cha)IGR, Mpr-LLGKK-NH₂, Mpr-LIGRK-NH₂, Mpr-LIGRKETQP-NH₂, Mpr-LLGKKDGTS-NH₂, (n-pentyl)₂-N-Leu-Ile-15 Gly-Arg-Lys-NH₂ and (Me-N-(n-pentyl)-Leu-Ile-Gly-Arg-Lys-NH₂, and the amidated or acylated forms thereof.

22. An isolated nucleic acid molecule which encodes a C140 receptor polypeptide or which is complementary to a DNA or RNA molecule encoding a C140 receptor polypeptide.

23. The nucleic acid molecule of claim 22 wherein said C140 receptor is the human C140 receptor.

- 57 -

24. A method to inhibit expression of C140 receptors in a cell comprising providing to said cell an oligonucleotide molecule which is antisense to, or forms a triple helix with, C140 receptor-encoding DNA or with DNA regulating expression of C140 receptor-encoding DNA, in an amount sufficient to inhibit expression of said C140 receptors, thereby inhibiting said expression.

25. A method to inhibit expression of C140 receptors in a subject, comprising administering to said subject an oligonucleotide molecule which is antisense to, or forms a triple helix with, C140 receptor-encoding DNA or with DNA regulating expression of C140 receptor-encoding DNA, in an amount sufficient to inhibit expression of said C140 receptors in said subject, thereby inhibiting said expression.

26. A pharmaceutical composition comprising an oligonucleotide molecule of claim 25 together with a pharmaceutically acceptable carrier or excipient.